CLAIMS

1. An isolated polynucleotide comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1-6 or degenerate variants thereof.

2. An isolated nucleic acid molecule comprising any one of the following:

(a) a nucleic acid sequence at least 90% identical to a nucleic acid sequence selected the group consisting of SEQ ID NOs: 1-6;

(b) a complement of the nucleic acid sequence of (a) above; or

(c) a fragment of the nucleic acid sequence of (a) or (b) above wherein the fragment comprises at least 20 nucleotides.

3. An isolated nucleic acid molecule comprising a nucleic acid sequence that hybridizes under stringent conditions to a hybridization probe, the nucleic acid sequence of which is selected from the group consisting of SEQ ID NOs: 1-6 or a complement thereof.

4. A promoter that drives expression, said promoter comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence shown in Figure 1, or a fragment or variant thereof;

(b) a nucleotide sequence having at least 80% identity to a nucleotide sequence set forth in Figure 1;

(c) a nucleotide sequence having at least 90 % identity to a nucleotide sequence set forth in Figure 1;

(d) a nucleotide sequence having at least 95 % identity to the nucleotide sequence set forth in Figure 1;

(e) a nucleotide sequence set forth in Figure 1;

(f) a nucleotide sequence having at least 10 contiguous nucleotides of a sequence set forth in Figure 1;

(g) a nucleotide sequence having at least 20 contiguous nucleotides of the sequence set forth in Figure 1; and

(h) a nucleotide sequence that hybridizes to the nucleotide sequence set forth in (a)-(g) above under stringent conditions.

5. The promoter of Claim 4, wherein said expression is constitutive.

6. A vector comprising a promoter as in Claim 7.

7. A host cell transfected or transformed with the vector of Claim 6.

8. The host cell of Claim 7, wherein said host cell is selected from the group consisting of HEK 293H, SV-40 transformed chondrocytes-C28A2, NIH3T3, human chondrosarcoma-SW1353 and HeLa cells.

9. A method of identifying an agent which alters interaction of an Agg-1 promoter gene of Claim 7 with a transcription factor binding agent comprising:

(a) contacting the Agg-1 promoter gene or a derivative or fragment thereof, the binding agent and with an agent to be tested;

(b) assessing the interaction of the Agg-1 promoter gene with the binding agent; and

(c) comparing the level of interaction with a level of interaction of the Agg-1 promoter gene or fragment thereof with the binding agent in the absence of the agent, wherein if the level of interaction of the Agg-1 promoter gene or derivative or fragment thereof in the presence of the agent differs, by an amount that is statistically significant, from the level of interaction in the absence of the agent, then the agent is an agent that alters interaction of the Agg-1 promoter gene with the binding agent.

10. The method of Claim 9, wherein said transcription factor binding agents comprise cytokines or growth factors.

11. The method of Claim 10, wherein said cytokines are selected from the group consisting of IL-1β and OSM.

12. The method of Claim 9, wherein said transcription factor binding agents inhibit transcription of said Agg-1 promoter.

13. The method of Claim 9, wherein said transcription factor binding agents induce transcription of said Agg-1 promoter.

14. The method of Claim 9, wherein said transcription factor binding agents bind to transcription factor binding sites selected from the group consisting of AP-1, STAT3 and NFkB.

15. An agent which alters interaction of an Agg-1 promoter gene of Claim 4 with a transcription factor binding agent, identifiable according to the method of Claim 9.

16. A method of identifying an agent which alters expression of Agg, comprising the steps of:

(a) contacting a solution containing a promoter region comprising a nucleic acid sequence as shown in Figure 1, operably-linked to a reporter gene, with an agent to be tested;

(b) assessing the level of expression of the reporter gene; and

(c) comparing the level of expression with a level of expression of the reporter gene in the absence of the agent, wherein if the level of expression of the reporter gene in the presence of the agent differs, by an amount that is statistically significant, from the level of expression in the absence of the agent, then the agent is an agent that alters expression of Agg.

17. The method of Claim 16, wherein said Agg is Agg-1.

18. A method for assaying a sample for the presence of an Agg-1 nucleic acid comprising:

(a) contacting said sample with a nucleic acid sequence comprising a contiguous nucleotide sequence, which is a at least partially complementary to a part of the sequence of an Agg-1 promoter gene under conditions suitable for hybridization; and

(b) assessing whether hybridization has occurred between the Agg-1 promoter gene and said nucleic acid sequence.

19. A reagent kit for assaying a sample for the presence of a Agg comprising in separate containers:

(a) one or more labeled nucleic acids comprising a contiguous nucleotide sequence which is at least partially complementary to a part of the nucleotide sequence of an Agg-1 promoter nucleic acid sequence; and

(b) reagents for detection of said label.

20. The reagent kit of Claim 19, wherein the labeled nucleic acid comprises a contiguous nucleotide sequences which is completely complementary to a part of the nucleotide sequence of said Agg-1 promoter nucleic acid.

21. A reagent kit for assaying a sample for the presence of metalloproteases comprising one or more nucleic acids comprising a contiguous nucleotide sequence which is at least partially complementary to a part of the nucleotide sequence of an Agg-1 promoter nucleic acid, and which is capable of acting as a primer for said Agg-1 promoter nucleic acid when maintained under conditions for primer extension.

22. The method of Claim 1, wherein the nucleic acid molecule is DNA.

23. The method of Claim 22, wherein the DNA is mammalian.

24. The method of Claim 23, wherein the DNA is human.

25. A method for producing an Agg-1 promoter comprising culturing a host cell of Claim 7 under conditions suitable for expression of the nucleic acid molecule and for translation of the resulting mRNA and recovering an expression product produced.

26. A method of screening for test compounds that regulate the activity of an Agg-1 promoter by:

(a) contacting a host cell in which the Agg-1 promoter disclosed herein is operably-linked to a reporter gene with a test medium containing the test compound under conditions which allow for expression of the reporter gene;

(b) measuring the expression of the reporter gene in the presence of the test medium;

(c) contacting the host with a control medium which does not contain the test compound but is otherwise identical to the test medium in (a), under conditions identical to those used in (a);

(d) measuring the expression of reporter gene in the presence of the control medium; and

(e) relating the difference in expression between (b) and (d) to the ability of the test compound to regulate the activity of the Agg-1 promoter.

27. A method of screening for transcriptional modulators of an Agg-1 promoter comprising:

(a) contacting a host cell in which the Agg-1 promoter disclosed herein is operably-linked to a reporter gene with an inducer or inhibitor of Agg-1 promoter activity under conditions which allow for expression of a reporter gene;

(b) measuring the expression of the reporter gene in the absence of the test compound;

(c) exposing the host cells to the test compound either prior to, simultaneous with, or after contacting, the host cells with the inducer;

(d) measuring the expression of the reporter gene in the presence of the test compound; and

(e) relating the difference in expression between (b) and (d) to the ability of the transcriptional regulator to modulate Agg-1 promoter activity.

28. A pharmaceutical composition comprising an Agg-1 promoter gene therapeutic agent of Claim 1.

29. The pharmaceutical composition of Claim 28, wherein the Agg-1 promoter gene therapeutic agent is an isolated nucleic acid molecule comprising a sequence as shown in Figure 1 or fragments or derivatives thereof.

30. A method of treating or delaying onset of disorders associated with articular degradation in an individual, comprising administering an Agg-1 promoter gene therapeutic agent to the individual, in a therapeutically effective amount.

31. The method of Claim 30, wherein said disorder is selected from the group consisting of inflammation, arthritis, rheumatoid arthritis, non-inflammatory arthritis osteoarthritis.

32. The method of Claim 30, wherein said degradation occurs in tissue selected from the group consisting of cartilage, synovial fluid and joints.

33. The method of Claim 30, wherein the therapeutic agent is an Agg-1 promoter gene antagonist.

34. A use of an Agg-1 promoter gene therapeutic agent in the preparation of a medicament for treating or delaying onset of disorders associated with articular degradation in an individual.

35. The use according to Claim 34, wherein said disorder is selected from the group consisting of inflammation, arthritis, rheumatoid arthritis and non-inflammatory arthritis osteoarthritis.

36. The use according to Claim 34, wherein said degradation occurs in tissue selected from the group consisting of cartilage, synovial fluid and joints.

37. The use according to Claim 34, wherein the therapeutic agent is an Agg-1 promoter gene antagonist.